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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/659,764	09/10/2003	Norman B. Javitt	1049-1-032N	4851

23565 7590 09/11/2007

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EXAMINER	
MAKAR, KIMBERLY A	
ART UNIT	PAPER NUMBER
1636	

MAIL DATE	DELIVERY MODE
09/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/659,764	JAVITT, NORMAN B.	
	Examiner	Art Unit	
	Kimberly A. Makar, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-16 and 18-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/06/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 1-20 are pending. Claims 1-15, 18-20 are withdrawn from a previous restriction requirement 1/17/07.

Election/Restrictions

2. Applicant's election with traverse of invention II in the reply filed on 6/11/07 is acknowledged. The traversal is on the ground(s) that the inventions are classified in the identical class/subclass, and that they have overlapping subject matter and does not require additional burdensome searches.

3. Applicants state:

> The method of Claim 17 and Group II is directed to identifying a compound/compounds capable of inhibiting the *expression* 27-hydroxy-7-dehydrocholesterol reductase, while the invention of Claim 16 and Group I is similarly directed to identifying a compound/compounds capable of inhibiting 27-hydroxy-7-dehydrocholesterol reductase *activity* (emphasis added).

4. This is not found persuasive because the methods were restricted between different class/subclasses (invention I was classified in class 435 subclass 7.1, whereas invention II was classified in class 436 subclass 94). Secondly, the invention I, encompassing claim 16 is directed to identifying a compound/compounds capable of inhibiting 27-hydroxy-7-dehydrocholesterol reductase activity is distinct from invention I encompassing claim 17, directed to identifying compounds capable of reducing 27-hydroxy-7-dehydrocholesterol reductase expression. It is possible to reduce the activity of 27-hydroxy-7-dehydrocholesterol reductase without also affecting its expression levels: potentially through dominant negative proteins that bind to active sites in the enzyme, or by preventing the enzyme from binding its target epitope. These

compounds are not necessarily the same as those that would be responsible for reducing 27-hydroxy-7-dehydrocholesterol reductase expression, which could be through inhibition of the promoter sequence of the gene, or through inhibiting upstream agonists of 27-hydroxy-7-dehydrocholesterol reductase. Thus the methods steps of preparing and testing the compounds can differ drastically, requiring additional burdensome searches.

The requirement is still deemed proper and is therefore made FINAL.

Specification

5. The disclosure is objected to because of the following informalities: the specification states the presence of a total of figures 1-7, however, only figures 1-3 appear to be included in the application (see page 7 of the instant specification).

Appropriate correction is required.

Abstract

6. Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:
(1) if a machine or apparatus, its organization and operation;
(2) if an article, its method of making;
(3) if a chemical compound, its identity and use;
(4) if a mixture, its ingredients;
(5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

7. The abstract of the disclosure is objected to because the abstract fails to mention the 27-hydroxy-7-dehydrochlosterol reductase. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

10. The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based on a single factor but rather is a conclusion reached by weighing many factors.

These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter., 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

11. 1) *The nature of the invention*. The invention involves measuring the affect of an agent compound on interfering with 27-hydroxy-7-dehydrocholesterol reductase activity by determining the level of the reductase or its encoding mRNA. In order for this screening method to be performed, the enzyme levels –either protein levels, or expression levels of mRNA must be measured.

12. 2) *Number of working examples and amount of direction or guidance present.* Applicants have provided no working examples of the measuring the activity of 27-hydroxy-7-dehydrocholesterol reductase by measuring the levels of the reductase or its encoding mRNA. All teachings directed towards the 27-hydroxy-7-dehydrocholesterol reductase appear to be prophetic. Applicants have not disclosed the identification of the gene that encodes the 27-hydroxy-7-dehydrocholesterol reductase, nor isolate the reductase enzyme, nor to produce antibodies specific for recognizing the enzyme, nor isolate the cDNA of the enzyme from a library in order to show that applicants are indeed able to measure the levels of the enzyme or its mRNA expression. The lone example applicants provide is the measurement of levels of cholesterol intermediates including 27-hydroxy-7-dehydrocholesterol – not the enzyme responsible for the intermediate production. Thus applicant measures the downstream products of such a reductase, but not the reductase directly. Applicants have not provided the nucleic acid sequence of such a reductase, nor the oligo sequences of primers that might be used to

such detection. Applicants have provided no nucleic acid sequences within the body of the specification, nor pointed to a Genbank or published article in which such sequences might appear. How much homology is there between the reductase of the instant claims and those known cholesterol hydroxylases? Is 27-hydroxy-7-dehydrocholesterol reductase conserved between species?

13. 3) *State of the art.* The art shows there is no disclosed 27-hydroxy-7-dehydrocholesterol reductase in the art. There is no disclosed protein sequence for a 27-hydroxy-7-dehydrocholesterol reductase in the literature at the present time. There is no mRNA sequence or genomic gene identified that encodes a 27-hydroxy-7-dehydrocholesterol reductase.

14. 4) *Unpredictability of the art.* The art is highly unpredictable. Without the disclosure of a known 27-hydroxy-7-dehydrocholesterol reductase amino acid sequences or nucleic acid sequence in the art, nor in the instant specification, the skilled artisan would be required to first identify and isolate, and reproduce the 27-hydroxy-7-dehydrocholesterol reductase in order to practice the claimed invention. Expression studies, in which tissues the reductase is expressed in, the regulation of the reductase, potential evaluation of reductase isoforms, etc. would all be required to be performed in order for the skilled artisan to make and use the claimed invention.

15. 5) *Level of skill in the art.* The level of skill is high. Because applicants have provided no data on the existence of a 27-hydroxy-7-dehydrocholesterol reductase other than the identification of the 27-hydroxy-7-dehydrocholesterol product, the skilled artisan would have to perform trial and error in order to actually produce the enzyme,

either in protein or nucleic acid form, in order to then practice the claimed invention of measuring either the levels of the enzyme or its mRNA.

16. 6) *The breadth of the claims.* The breadth of the claims are broad. The claims read on a method of measuring the amount of an unidentified enzyme or its encoding mRNA, neither of which have been disclosed in the art nor by applicant. There is no determination of what type of compounds are to be screened nor how to determine what threshold a compound "interferes" with inhibiting the expression of 27-hydroxy-7-dehydrocholesterol reductase.

17. Given the above analysis of the factors which the courts have determined are critical in ascertaining whether a claimed invention is enabled, including the highly unpredictable art, the scarcity of working examples provided by applicant, the lack of guidance by the applicant, and the broad nature of the invention it must be considered that the skilled artisan would have to conduct undue and excessive experimentation in order to practice the claimed invention.

18. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

19. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 17 is directed towards a screening method for identifying agent compounds capable of interfering with the expression of 27-hydroxy-7-dehydrocholesterol reductase activity, comprising determining the level of 27-hydroxy-7-dehydrocholesterol reductase or its encoding mRNA. It is unclear from the specification

from the claims and the specification, what enzyme is actually being measured. Applicants do not provide any data on the measurement of a 27-hydroxy-7-dehydrocholesterol reductase or its encoding mRNA. Are applicants claiming to determine the levels of 27-hydroxylase that acts on 7-dehydrocholesterol? Are applicants claiming to determine levels of 7-hydroxylase that acts on 27-hydrocholesterol? Or, is there a specific enzyme that works on both C27 and C7 of cholesterol? It is unclear from the specification and the claim what enzyme is being measured, either direct measurement of the enzyme levels, or its encoding mRNA? A skilled artisan would be unable to determine the metes and bounds of the claimed invention.

Conclusion

20. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Makar, Ph.D. whose telephone number is 571-272-4139. The examiner can normally be reached on 8AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D. can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kam/09/01/07

/Daniel M. Sullivan/
Primary Examiner
Art Unit 1636